The influence of the sympathetic nervous system through the $\alpha_2C$ adrenergic signalling pathway in Breast cancer Bone metastasis

Ana Fonseca1,2,3,a, Sofia Tojol1,3,4,a, Francisco Conceição1,3,4, a; Daniela M. Sirescl1,2, a, Meriem Lamghari1,2, a (lamghari@ineb.up.pt)

1-Instituto de Investigação e Inovação em saúde (I3S), Universidade do Porto, Portugal; 2-Instituto Nacional de Engenharia Biomédica (INEB), Universidade do Porto, Portugal; 3-Faculdade de Engenharia da universidade do Porto, Portugal; 4-Instituto de Ciências Biomédicas Abel Salazar (ICBAS), Universidade do Porto, Portugal

Introduction
Breast cancer (BC) patients are at higher risk of suffering from psychological distress, as chronic stress. In fact, in these cases the sympathetic nervous system (SNS) hyperactivation have been associated in the progression of BC and homing to the bone microenvironment, via $\alpha_2C$-adrenergic signalling pathway [1]. A recent study has also related a possible contribution of $\alpha_2C$-adrenergic signalling pathway [2], adding another layer of complexity on the intricate interactions between SNS activation and bone-tumour niche.

Aim
- The aim of this work is to understand the effect of the sympathetic nervous system through the $\alpha_2C$ - ADR pathway in breast cancer bone metastasis.

Methodology
1. Mouse osteoclast isolation, differentiation and resorptive activity

2. Effect of the $\alpha_2C$ - ADR pathway in the bone niche

3. In vivo model of breast cancer bone metastasis

References

Preliminary Results

Monoculture mOC

Co-culture mOC/OBs

Figure 1 - mOC and mOC/OB culture optimization and characterization. A) Morphology of the monoculture of mOC. B) Resorptive activity of the monoculture of mOC C) Morphology of the coculture of mOC/UAMS. D) Resorptive activity of osteoclast in the coculture

$\alpha_2C$ – ADR Indirect effect

$\alpha_2C$ – ADR Direct effect

Figure 2 - Resorptive activity of the mOC when treated with CM retrieve from 4T1.2 cells

Figure 3 - Resorptive activity of the mOC in the coculture when treated with different NE concentrations. Effect of the $\alpha_2C$ - ADR pathway in the pit, trench and trap activity of the mOC in coculture

Conclusion
The $\alpha_2C$-ADR pathway seems to have impact on the bone niche as:
- Osteoclast activity is decreased when the receptor is blocked
- Osteoblast have also a slight decrease in the RANKL expression

However the sympathetic innervation of the tumour was scarce. Further work needs to be performed to increase the number of samples

Acknowledgements
This work was financed by Portuguese funds through FCT/MCTES in the framework of the project “SensOC” (POCI-01-0301-IFI-040158), PTDC/MED-PAT/30158/2017/F.C. is a recipient of the PhD fellowship SFRH/BDE 128771/2017. D.M.S is a recipient of the postdoctoral fellowship SFRH/BPD/115341/2016